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Measuring Light at Night and Melatonin Levels in Shift Workers: A Review of the Literature

Claudia M. Hunter, PhD[1] and **Mariana G. Figueiro, PhD**[1]

[1]Lighting Research Center, Rensselaer Polytechnic Institute, Troy, NY, USA

Abstract

Shift work, especially that involving rotating and night shifts, is associated with an increased risk of diseases, including cancer. Attempts to explain the association between shift work and cancer in particular have focused on the processes of melatonin production and suppression. One hypothesis postulates that exposure to light at night (LAN) suppresses melatonin, whose production is known to slow the development of cancerous cells, while another proposes that circadian disruption associated with shift work, and not just LAN, increases health risks. This review focuses on six studies that employed quantitative measurement of LAN and melatonin levels to assess cancer risks in shift workers. These studies were identified via searching the PubMed database for peer-reviewed, English-language articles examining the links between shift work, LAN, and disease using the terms *light at night, circadian disruption, health, risk, cancer, shift work,* or *rotating shift.* While the results indicate a growing consensus on the relationship between disease risks (particularly cancer) and circadian disruption associated with shift work, the establishment of a direct link between LAN and disease has been impeded by contradictory studies and a lack of consistent, quantitative methods for measuring LAN in the research to date. Better protocols for assessing personal LAN exposure are required, particularly those employing calibrated devices that measure and sample exposure to workplace light conditions, to accurately assess LAN's effects on the circadian system and disease. Other methodologies, such as measuring circadian disruption and melatonin levels in the field, may also help to resolve discrepancies in the findings.

Keywords

breast cancer; light at night; health; circadian disruption; melatonin production; shift work; rotating shifts

The incidence of breast cancer in Western industrialized society increased throughout the 20th century and into the 21st (Chu et al., 1996; Ghafoor et al., 2003). Environmental

Corresponding Author: Mariana G. Figueiro, PhD, Lighting Research Center, Rensselaer Polytechnic Institute, 21 Union Street, third floor, Troy, NY 12180, USA. figuem@rpi.edu.

Author Contribution

Claudia M. Hunter and Mariana G. Figueiro contributed to acquisition, analysis, and interpretation drafted manuscript critically revised manuscript gave final approval agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests

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factors, such as light at night (LAN), acting through endocrine disruption, have been implicated in this increase in risk (Stevens & Rea, 2001). A series of studies have shown that light–dark patterns incident on the retina set the timing of the master clock (Moore-Ede, Sulzman, & Fuller, 1982). Circadian disruption resulting from chronic exposure to irregular light–dark patterns plays a role in diseases such as cardiovascular disease, diabetes, obesity, and tumor growth (Filipski et al., 2002, 2003; Fu & Lee, 2003; Fu, Pelicano, Liu, Huang, & Lee, 2002).

The master clock in the human suprachiasmatic nuclei (SCN) is genetically preprogrammed to run for about 24.2 hr, although individuals differ in the precise timing of their own master clocks. For those working during the day and sleeping at night, daily morning light upon waking synchronizes the timing of the master clock to local times on earth. Specifically, light falling on the retina provides the synchronizing signal to the SCN, which then run on a 24-hr solar schedule rather than the preprogrammed 24.2-hr schedule. However, the characteristics of lighting that affect our circadian system are different from those that affect our visual system (Rea, Figueiro, & Bullough, 2002). Indoor illumination, moreover, is designed for the needs of the visual system, not the circadian system. Exterior light levels during the day, even under cloud cover or during the winter, are much higher than those now found in windowless, electrically illuminated buildings. Natural light is also dominated by short-wavelength radiation, particularly from the blue sky. Most obviously, daylight is only present during the day, and the timing of bright days and dark nights is, by definition, perfect for regulating the human circadian system.

The built environment has also changed the patterns of our light–dark exposure. The absence of suitable light in built interiors may induce “circadian darkness,” which in turn may negatively affect entrainment of our circadian system. This effect occurs because electric lighting typically found in indoor environments can be insufficient to stimulate and synchronize the circadian clock to the day–night cycle (McIntyre, Norman, Burrows, & Armstrong, 1989; Rea et al., 2002). In addition, people tend to shift their daily schedules later into the night than was the custom before the introduction of electricity. More importantly, electric lighting enables 24-hr operations that require humans to stay awake at night, when their biological clock is telling them to sleep.

If we are not exposed to appropriate light to promote circadian entrainment, a harmony that should exist between the timing of our preprogrammed clock and the local, solar light–dark pattern is broken. When that harmony is broken, disturbances in a number of bodily functions begin to appear—for example, after transcontinental air travel. Disruption of the circadian cycle, either by melatonin depletion or by exposure to irregular light–dark cycles, has been shown to affect mortality in some animal models (Blask et al., 2005; Filipski et al., 2003, 2004; Stevens et al., 2007). Most people in modern societies now probably experience circadian disruption by dim, extended, aperiodic light exposure. We no longer expect everyone to spend their waking days under the blue sky and to sleep throughout the entire night in total darkness. Thus, lack of entrainment of the circadian system could be an important biophysical mechanism underlying the increased incidence of breast cancer in our industrialized, 24-hr society.

One population at greater risk for exposure to LAN and irregular light–dark patterns comprises shift workers working evening and night shifts. In fact, epidemiological studies show that this population is at increased risk for diseases, especially cancer (Carter, Diver, Hildebrand, Patel, & Gapstur, 2014; Davis, Mirick, & Stevens, 2001; Megdal, Kroenke, Laden, Pukkala, & Schernhammer, 2005; Schernhammer, Feskanich, Liang, & Han, 2013; Schernhammer et al., 2003). Researchers have proposed two competing hypotheses to explain the association between shift work and cancer risks. Stevens (1987) proposed the original hypothesis, referred to as the "melatonin hypothesis." Melatonin, a hormone that is produced at night and in darkness, and whose secretion is regulated via light–dark patterns that are detected by the retina and transduced to the SCN, has been shown to act directly as a free-radical scavenging molecule (Reiter, Tan, & Fuentes-Broto, 2010). In his original hypothesis, Stevens (1987) postulated that melatonin production decreases the amount of circulating estrogen, which would then slow the development and turnover of breast epithelial stem cells that could become cancerous. We know generally that LAN can suppress the nocturnal production of melatonin, but research has yet to establish the specific amount of LAN required to suppress melatonin. The second hypothesis, initially postulated more than a decade later, proposes that circadian disruption resulting from rotating shift work, not simply acute melatonin suppression by LAN, increases cancer risks (Haus & Smolensky, 2013; Truong et al., 2014). To test this latter hypothesis, it is also important to measure circadian disruption in the field.

A number of observational studies have suggested that shift work, especially when involving rotating shifts with nighttime work, is associated with an increased risk in breast and other kinds of cancer, potentially mediated through melatonin suppression by exposure to LAN. For example, Bhatti, Cushing-Haugen, Wicklund, Doherty, and Rossing (2013) found that increasing nights of shift work produced significantly elevated risk of ovarian cancer. Having ever worked night shifts elevated the risk of invasive ovarian tumors by 24% and borderline tumors by 48%. Carter, Diver, Hildebrand, Patel, and Gapstur (2014) retrospectively examined data from the American Cancer Society's Cancer Prevention Study II. They found that women who had reported working rotating shifts in 1982 had a somewhat elevated risk (relative risk [*RR*] = 1.27) of dying from ovarian cancer, but women who worked fixed night shifts did not. Working rotating shifts also significantly affected the odds of developing colorectal cancer in women from the Nurses' Health Study II (Schernhammer et al., 2003). For women who had worked 15 or more years on rotating shifts, the odds were 1.35 times greater than for women who had never worked rotating shifts. There was, however, no odds increase for working rotating shifts up to 14 years. Schernhammer, Feskanich, Liang, and Han (2013) also studied the effects of rotating shift work on risk for lung cancer. The odds risk (*OR*) was 1.28 for women who had worked 15 or more years on rotating shifts but only for current smokers. The risk was highest for women smokers to develop small-cell lung cancers (*OR* = 1.56) and squamous-cell lung cancers (*OR* = 1.44). Davis, Mirick, and Stevens (2001) found links between shift work and breast cancer. In their study, 813 women with breast cancer (BC) gave detailed interviews about their work schedule, sleep habits, lighting conditions at home during sleep hours, and other risk factors. BC risk increased with each night of nonpeak sleep (*OR* = 1.14 per night), defined as going to sleep after 02:00, awakening for the day before 01:00, or simply not

going to bed and instead relying on naps. The *OR* was 1.7 for at least 2.6 nights of nonpeak sleep per week, but the ratio did not increase with additional nights. Women who had worked the graveyard shift at least once in the preceding 10 years had an elevated risk of BC (*OR* = 1.6), and the risk increased with each additional hour per week (*OR* = 1.06 per hr/week). Women who had worked at least 5.7 hr/week on the graveyard shift had more than twice the risk of developing BC (*OR* = 2.3).

In a meta-analysis summarizing current observational studies, including several studies of flight attendants, authors suggest there is a 50% increased risk of BC associated with night-shift work (Megdal et al., 2005). More recently, however, Kolstad (2008) reviewed the literature and concluded that there was insufficient evidence to support an association between night-shift work and BC risk. Consistent with Kolstad's conclusion, Kamdar, Tergas, Mateen, Bhayani, and Oh (2013) published a systematic review and meta-analysis of 15 studies, concluding that there was only weak evidence to support the association between night-shift work and BC risk and, more importantly, that there was no evidence for a dose relationship between night-shift work and BC risk.

One explanation for the contradictory results might be the lack of, or inconsistent methods employed for, measurement of LAN. In the present review, therefore, we summarize original research articles detailing studies that use some form of quantitative measurement of LAN to correlate with or predict health risk in shift workers, particularly with respect to cancer. In the majority of these studies, researchers also collected melatonin (or its metabolite) levels in an attempt to establish a more direct relationship between LAN and melatonin suppression in this population. Of specific interest is the amount and duration of LAN, or the duration of shift work, required to cause circadian disruption and/or melatonin suppression, thereby leading to increased cancer risk.

Methods

We searched the PubMed database for peer-reviewed articles published in English (through 2015) that examined the links between shiftwork, LAN, and cancer. The search terms *light at night* combined with *health* or *risk* yielded 259 articles. *Light at night* and the specific term *cancer* yielded 144 articles. The terms *light at night* and *shift work* or *rotating shift* yielded 84 articles. The exclusion of redundant and/or duplicate items from these searches left a total of 244 articles. The terms *circadian disruption* combined with *health* or *risk* yielded 302 articles, and the terms *circadian disruption* and *cancer* yielded another 215 articles. The exclusion of redundant and/or duplicate articles between these searches resulted in a total of 263 articles.

We also searched specifically for articles that examined melatonin suppression resulting from exposure to LAN. The term *light* combined with *night*, *melatonin*, and *suppression* yielded 165 articles. The exclusion of articles that did not report specific light levels and duration of exposure with respect to their effects on human participants resulted in a total of 20 articles.

In all, our literature search identified 527 articles for consideration. We excluded articles that reviewed existing literature. We did not include studies on certain classes of shift workers, such as airline personnel, whose work entails exposure to causes of circadian disruption other than LAN (e.g., jet lag, sleep deficit, etc.). We also excluded studies of genetic markers and polymorphisms. The criteria for inclusion in this review limited our final selection to six original research articles detailing epidemiological studies of cancer risk in human participants, specifically shift workers, where either their exposure to LAN was quantitatively assessed in some way or their levels of melatonin (or its metabolites) were quantitatively measured over a relevant period (see Table 1).

Results

Grundy et al. (2009) examined melatonin production in 61 nurses working rotating shifts on a schedule of two 12-hr day shifts, two 12-hr night shifts, and then 5 days off. The nurses were divided into two groups that participated in two discrete test periods. The first period consisted of two 12-hr day shifts, the second consisted of two 12-hr night shifts, and each was preceded by a 24-hr melatonin assessment during which nurses completed a diary and a study questionnaire. Each shift, whether day or night, was separated from the next and preceding shifts by at least 12 hr off. Participants wore light loggers that measured illuminance in photopic lux at 5-min intervals. Briefly, illuminance is irradiance weighted by the photopic luminous efficiency function ($V(\lambda)$), an orthodox measure of the spectral sensitivity of the human fovea, peaking at 555 nm. Participants wore the light loggers around their necks during waking hours and placed them on bedside tables when they were sleeping. When participants were bathing, showering, or swimming they removed the light loggers. Results demonstrated that nurses working night shifts experienced significantly more light exposure during their reported sleep times than those working day shifts (45.49 lux vs. 6.26 lux), most likely because their bedrooms were not completely dark during the daytime. In addition, levels of urinary 6-sulfatoxymelatonin (aMT6s), a major metabolite of melatonin, measured from urine samples collected upon waking (between 05:00 and 07:00 for day shift workers and between 15:00 and 17:00 for night shift) were significantly lower (7.64 ng/mL vs. 20.98 ng/mL) in nurses working night shift. Peak melatonin levels measured from saliva samples occurred at night for both groups, day and night shifts. Together, these results suggest, contrary to the authors' expectations, that the observed difference in aMT6s levels between the two shifts reflects the fact that night-shift workers do not have peak melatonin levels while sleeping during the day.

Grundy, Tranmer, Richardson, Graham, and Aronson (2011) established four 48-hr periods in which they asked participants to collect data while working one day and one night shift during both winter and summer. During each period, participants were asked to wear a light logger around their neck during waking hours and to provide four saliva and two urine samples (upon waking) over a 24-hr period. The authors found that, while rotating-shift nurses were exposed to significantly more light between midnight and 05:00 when they were working their night shifts, their melatonin and estradiol levels were not significantly different from their day-shift levels. Consistent with their previous study (Grundy et al., 2009), the participants' peak melatonin levels occurred during the nighttime when they were working both day and night shifts. Moreover, light exposure was not significantly associated

with either peak melatonin or change in melatonin levels observed between the two shifts. The researchers attributed their study's failure to find melatonin suppression to the fact that the maximum LAN level the nurses experienced was 37.2 lux, which is below the 80-lux level shown to have an effect on melatonin production (Figueiro, Rea, & Bullough, 2006; Zeitzer, Dijk, Kronauer, Brown, & Czeisler, 2000).

Dumont, Lanctot, Cadieux-Viau, and Paquet (2012) measured melatonin production and exposure to LAN in a study on the effects of shift work. The goal of the study was to test the hypothesis that total melatonin production decreased when participants were working nights as compared to when they were working day/evening shifts. They tracked 13 (3 males, 10 females, with a mean age of 36.3 years) rotating-shift workers' excretion of aMT6s and their light exposure with an ambulatory light meter during two 48-hr periods, one while they were working a night shift and one a day shift. All participants were working a full-time schedule that included at least three consecutive night shifts. The data collection usually occurred during the second and third shifts worked in a series of three to seven consecutive night or day/evening shifts. Participants wore a light meter, similar to a medallion, around their necks at all times while awake (except for showering and sports) and placed them face up on their bedside tables during sleep. The researchers found no significant difference in either melatonin excreted or light exposure experienced between the two shifts (night shift: 72.5 ± 54.9 lux; day/evening shift: 64.7 ± 50.8 lux) nor did they find a correlation between melatonin production and light exposure within a given work shift. The latter finding might be explained by the fact that the light levels in this study averaged only 73 lux during work periods. The researchers did, however, find an inverse correlation between melatonin production and LAN exposure. The workers produced significantly less melatonin over the total 24-hr period that included their night shift than they did in the 24-hr period that included their day shift. In other words, while the authors did not observe an acute suppression of melatonin in night-shift workers, they did observe a possible partial phase shift of the melatonin rhythms, which suggests the start of the re-entrainment of the workers' circadian rhythms to the night shift. This process of reentrainment would cause a transitory period of internal desynchronization of circadian rhythms (i.e., circadian disruption). These results are the first to suggest that acute melatonin suppression alone may not be sufficient to explain the association between LAN and increased cancer risks in shift workers.

Papantoniou et al. (2014) examined the relationships between melatonin, shift status, and light exposure in 75 night and 42 day workers. Participants were asked to collect samples from all voids over the course of a 24-hr period and wore light data loggers at shoulder level during waking hours (light loggers were placed on a bedside table during sleeping periods). In contrast to the studies discussed earlier, the authors found that night-shift workers experienced more than 3 times as much mean light exposure as day-shift workers (192 lux for night-shift workers and 57 lux for day-shift workers) from 22:00 to 07:00. Overall, night-shift workers produced 33.8% less melatonin than day-shift workers during the 24-hr study period. For night-shift workers who had a daytime diurnal preference, melatonin levels were 53.7% lower than those of day-shift workers. Workers who had been on night shift 4 or fewer times in the previous 2 weeks had melatonin levels 40.6% lower than those of day-shift workers, but as the number of recent night shifts increased, suppression was less acute (with nine or more night shifts, melatonin was only 22.9% lower). This trend toward less

suppression suggests that the participants were becoming adapted to night work, phase shifting their circadian rhythms.

Dumont and Paquet (2014) found a progressive decrease in melatonin production when 38 participants (15 males and 23 females, with a mean age of 26.6 years) worked a simulated night shift covering three consecutive 24-hr periods (preceded by a 24-hr period with one simulated day shift). The researchers shifted the circadian phase in the participants by exposing them to varying profiles of daytime lighting (150–1,800 lux while awake and 2–20 lux while asleep). The groups were partial phase advance, partial phase delay, and stable phase. From the first day shift through the last night shift, the amount of excreted aMT6s fell, reaching a significant decline by the last night. It also fell during each 24-hr period, reaching significant declines on the second and third periods. Excretion did not vary by phase-shifted group, however. The fact that melatonin was not significantly reduced until the end of the third night shift probably indicates that melatonin was not acutely suppressed by the light level researchers used during the simulated shift (50 lux), which was representative of many night-shift work-places such as nursing stations. Rather, the authors suggest that the gradual decline in melatonin levels reflected the gradual phase shift of the daily episode of melatonin production. They also note that the participants slept less and had lower sleep efficiency during the study relative to baseline measures for nighttime sleep described for the study in a related publication (Chapdelaine, Paquet, & Dumont, 2012), which might also have led to lower melatonin production.

Burch, Yost, Johnson, and Allen (2005) measured and compared melatonin production, light exposure, and physical activity levels among 165 manufacturing workers (107 males and 58 females) on three nonrotating shifts: first (6:00–14:00), second (14:00–22:00), and third (22:00–6:00). Over a single 24-hr period, investigators assessed the participants' melatonin production via the measured concentrations of 6-hydroxymelatonin sulfate (6-OHMS), a major urinary metabolite, in postshift and postsleep urine samples. They monitored light exposure and physical activity levels over the same period using wrist-worn loggers and calculated time-weighted average (TWA) light exposure for six periods (home-morning, prework commute, work, postwork commute, home-evening, and sleep). Second-shift workers were exposed to considerably more ambient light over the 24-hr period, reaching a TWA light exposure of 1,338 lux, compared to workers on the first (770 lux) and third (427 lux) shifts. The participants' melatonin concentrations over the same period, measured as adjusted mean sleep-work ratios of 6-OHMS concentration normalized to urinary creatinine levels (6-OHMS/cr), were very similar between the first (ratio = 4.2) and the second (ratio = 4.5) shifts but lower for the third shift (ratio = 2.3). Moreover, the proportion of workers with mean ratios of ≤1 in the second shift (11%) was elevated compared to the first shift (8%), although the elevation was not statistically significant; the proportion noted for the third shift (25%) was more than 3 times greater than that noted for the first shift. Burch et al. (2005) concluded that adjusted mean sleep–work 6-OHMS/cr ratio is a good predictor of melatonin phase shift and sleep disruption and that low ratios (especially ≤1) are associated with higher incidences of self-reported mental symptoms (which, according to the authors, included concentration, dizziness, headaches, and memory), sleep symptoms, and fatigue.

Discussion

The LAN hypothesis forwarded by Stevens (1987) has stimulated a series of animal and epidemiological studies. The animal studies to date strongly suggest that both acute melatonin suppression by LAN and circadian disruption resulting from irregular light–dark patterns are associated with an increased rate of tumor growth and increased mortality in animals (Blask et al., 2005; Filipski et al., 2003, 2004; Stevens et al., 2007). A large number of epidemiological studies also suggest an association between working rotating shifts for 20–30 years and cancer risks (reviewed in Megdal et al., 2005), but there are a few studies that have failed to confirm this relationship (reviewed in Kolstad, 2008, and Kamdar, Tergas, Mateen, Bhayani, & Oh, 2013). Given the limited human evidence in tandem with the sufficient evidence in experimental animals, in 2007, the International Agency for Research on Cancer (IARC) classified “shift work that involves circadian disruption” as a probable human carcinogen, Group 2A. Since the IARC report in 2007, additional published studies have added support to an epidemiological link between shift work and cancer risks (Åkerstedt et al., 2015; Bonde et al., 2012; Cordina-Duverger et al., 2016; Lin et al., 2015; Papantoniou et al., 2015).

Despite this growing support, however, a direct link between LAN, acute melatonin suppression or circadian disruption, and cancer risks in shift workers has still not been firmly established, most likely due to a lack of quantitative assessment of LAN and melatonin levels in the field (Ijaz et al., 2013). In fact, only a very limited number of studies have measured personal light exposures in shift workers and related these exposures to their melatonin levels. More importantly, however, none of the studies we reviewed here used calibrated light meters that measure light as it affects the human circadian system (Figueiro, Hamner, Bierman, & Rea, 2013). It is now well accepted that the photopic luminous efficiency function, which most commercially available photometers employ, does not represent the spectral response of the human circadian system, which is maximally sensitive to short wavelengths (i.e., blue light; Brainard et al., 2008; Glickman, Levin, & Brainard, 2002; Kozaki, Koga, Toda, Noguchi, & Yasukouchi, 2008; Rea, Figueiro, Bullough, & Bierman, 2005; Thapan, Arendt, & Skene, 2001). In addition, the studies included in this review did not cover in detail the spectral characteristics of the observed light sources and described absolute light levels only in general terms, such as “bright white” or “normal room lighting.” Given that the human visual system is more sensitive to light than the human circadian system (Rea et al., 2002), researchers should avoid using qualitative references to the lighted environment.

As reviewed in this article, three studies conducted in real-world settings (Dumont, Lanctot, Cadieux-Viau, & Paquet, 2012; Grundy et al., 2009; Grundy, Tranmer, Richardson, Graham, & Aronson, 2011) showed that light levels at work were below what is required for the activation of the circadian system (<80 lux; Zeitzer et al., 2000). In one study, in which workers received an average of 73 lux at work, nighttime melatonin levels were not significantly affected by night-shift work, but the total 24-hr melatonin concentrations were lower in night-shift workers compared to daytime workers. In a fourth study, in which researchers assessed light exposures at shoulder level and measured urinary aMT6s concentrations in night-shift and day-shift workers, the mean LAN exposures ranged from

15 to 246 lux over the entire night shift. Between midnight and 05:00, workers experienced a median light level of 38 lux (Papantoniou et al., 2014). Despite the low light levels, the authors found, after controlling for potential confounders, that night-shift workers had 33.8% lower aMT6s concentrations than day-shift workers, and their peak levels occurred 3 hr later than in the day-shift workers. Interestingly, the greater the number of consecutive nights worked, the greater the reduction in aMT6s concentrations.

One interesting finding from several of the reviewed studies is that working night shifts reduced overall melatonin amplitude even in the absence of evidence for acute melatonin suppression during the night shift. This finding suggests that shift workers go through a slow adaptation over the course of the week that results in a lower nighttime melatonin amplitude, which in turn suggests that circadian disruption, rather than acute melatonin suppression by LAN, is associated with some of the health risks in working shifts.

Other methodological issues that may explain the findings of the studies reviewed here relate to the measurement of circadian disruption in the field. One way to improve study of the correlation between LAN and circadian disruption might be to calculate phasor magnitude, a metric proposed by Rea, Bierman, Figueiro, and Bullough (2008) and Miller, Bierman, Figueiro, Schernhammer, and Rea (2010). Phasor magnitude is a measure of circadian entrainment; it correlates circadian light–dark exposures with activity–rest levels. Greater phasor magnitude indicates greater synchronization of the activity–rest cycle with the light–dark pattern. Light levels and activity can be simultaneously measured with a Daysimeter, which is a novel personal, calibrated light meter device (Figueiro et al., 2013; Rea, Bierman, Figueiro, & Bullough, 2008). Phasor analysis has successfully demonstrated that circadian disruption increased with each additional night shift worked by nurses on rotating shifts (Miller, Bierman, Figueiro, Schernhammer, & Rea, 2010). Another possible way to measure circadian disruption in the field is that used by Burch et al. (2005), who proposed that the adjusted mean sleep–work 6-OHMS/cr ratio might be a good indicator of circadian disruption. Future studies should test some of these metrics in the field.

The importance of the LAN–cancer connection will undoubtedly motivate researchers conducting future longitudinal studies of shift workers to devise better protocols for assessing LAN exposure. One key point is that personal light exposures should be measured using calibrated devices that measure LAN as it impacts the circadian system rather than the visual system (photopic lux levels). Although it is unlikely that shift workers could wear calibrated light meters for long periods, studies could be designed to sample their workplace light conditions and circadian entrainment at significant mile-posts, allowing more accurate extrapolation of the effect of circadian disruption on future health outcomes. Another alternative would be for researchers to calibrate subjective scales using personal, calibrated sensors in a smaller group of people prior to using questionnaires in a larger group of workers.

In summary, although there is a growing consensus on the relationship between disease risks (particularly cancer) and circadian disruption associated with shift work, the establishment of a direct link between LAN and disease has not been established. This gap is most likely due to a lack of consistent, quantitative methods for measuring LAN in the research to date.

Future research must address this gap by developing more precise methods of measuring LAN, light exposure more generally, and circadian disruption.

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Table 1

Summary of Studies Measuring Light at Night (LAN) and Levels of Melatonin or Its Metabolites in Shift Workers.

Author/Year	Objective	Sample Size/Characteristics	Methods	LAN Metric	Results
Burch, Yost, Johnson, & Allen (2005)	Examine melatonin production in shift workers; correlate with sleep disruption and other sleep complaints	165 nonrotating shift workers; 58 females and 107 males; mean ages between 29 ± 9 (third shift) and 38 ± 12 (first shift) years	Participants worked 1 of 3 nonrotating shifts: first (6:00–14:00), second (14:00–22:00), or third (22:00–6:00). Each gave 1 urine sample immediately after shift and 1 after waking. Adjusted mean sleep–work 6-OHMS/cr ratios calculated. LE and physical activity levels monitored via data loggers. TWA 24-hr LE calculated, LAN exposure not reported	Ambient light and physical activity levels recorded via wrist-worn Actiwatch-L logger (Mini Mitter, Inc., Bend, OR) every 15 s for 24-hr study period	Second-shift workers experienced 24-hr TWA LE of 1,338 lux, compared to 770 lux (first shift) and 427 lux (third shift). First and second shift had comparable sleep–work 6-OHMS/cr ratios (adjusted ratio 4.2 and 4.5, respectively.); third-shift ratio only 2.3. Proportion of workers with ratio ≤ 1.0 in third shift almost three times greater than in first shift (25% vs. 8%). Mean LE for third shift ranged from 15 to 246 lux (median, 38 lux) between 00:00 and 05:00. Study concluded that adjusted mean sleep–work 6-OHMS/cr ratio was a good predictor of melatonin phase shift and sleep disruption. Ratios ≤ 1 were associated with higher reporting of mental symptoms, sleep symptoms, and fatigue
Dumont, Lanctot, Cadieux-Viau, & Paquet (2012)	Correlate melatonin levels and LAN; compare night and day shifts; test hypothesis that melatonin production decreases on night shift	13 rotating-shift workers; 10 females and 3 males; mean age 36.3 ± 9.2 years	Participants studied in two 48-hr periods, 1 including 1 night shift and the other including 1 day shift. All participants full time, working ≥ 3 successive night shifts. Excretion of urinary aMT6s measured during work, leisure, and sleep episodes	Ambulatory light levels measured via Actiwatch-L logger (Mini Mitter, Inc., Bend, OR) worn around neck continuously except during sleep (when placed face up on bedside table), bathing, and sports	No significant difference in LE and total aMT6s excretion between shifts, approximately the same number of participants in each group showed decreased/increased aMT6s excretion. However, participants produced significantly less melatonin over the 24-hr periods that including night shifts than the 24-hr period that included day shift. Study suggests acute melatonin suppression alone may not be sufficient to explain association between LAN and shift workers' increased cancer risks
Dumont & Paquet (2014)	Measure nighttime and 24-hr melatonin levels, simulated night shift	38 participants; 15 males and 23 females; mean age 26.6 ± 4.2 years	Participants worked simulated day and night shifts for 6-day study. Collected salivary dim-light melatonin onset first and last day, excretion of urinary aMT6s every 2 hr. Simulated working 1 day and 3 night shifts over 4 days	Work-environment light level set at 50 lux for 1 day and 3 successive simulated night shifts	Melatonin progressively decreased over 3 night shifts, reaching significance on third night. Effects strongest in women on oral contraceptives. Melatonin probably not directly suppressed by low light levels (50 lux); rather, by circadian disruption
Grundy et al. (2009)	Explore effects of LAN exposure, sleep duration, and physical activity on melatonin levels in rotating-shift workers in cross-sectional study	61 rotating-shift female nurses, Kingston, Ontario; 30–65 years old; divided into 2 age-distributed groups	Participants working rotating shifts (two 12-hr days, two 12-hr nights, 5 days off) participated for 3 days (either day or night shift). Self-reported physical activity and sleep duration collected via questionnaires and diaries. Provided 1 urine and 4 saliva samples for melatonin analysis	Light data logger worn around neck while not in bed or while bathing. Light levels measured every 5 min over 3-day period	Night-shift workers' LE significantly higher during sleep times than day-shift workers' (45.49 lux vs. 6.26 lux) and aMT6s levels significantly lower (7.64 ng/mL vs. 20.98 ng/mL). Peak melatonin levels occurred at night for both groups. Results suggest, contra authors' expectations, difference in aMT6s levels reflects night-shift workers not having peak melatonin while sleeping during day
Grundy, Tranmer, Richardson, Graham, & Aronson (2011)	Explore effects of LAN exposure on melatonin levels in rotating-shift workers	123 rotating-shift female nurses, Kingston, Ontario; mean age 40.5 years	Participants working rotating shift (two 12-hr days, two 12-hr nights, 5 days off) participated during 1 night and 1 day shift in both winter and summer. Provided 4 saliva and 2	Light data logger worn around neck during waking hours and placed on bedside table when sleeping. Levels	Rotating-shift workers received more LE when working night shift; melatonin and estradiol levels not significantly different from day-shift levels. Peak melatonin levels occurred during nighttime, regardless of shift worked. LE not

Author/Year	Objective	Sample Size/Characteristics	Methods	LAN Metric	Results
			urine samples over 24-hr period within each 48-hr session	measured every minute throughout 48-hr period	significantly associated with peak melatonin or melatonin level changes between 2 shifts. Failure to find melatonin suppression because maximum LAN level experienced was 37.2 lux, below 80-lux level that affects melatonin production
Papantoniou et al. (2014)	Correlate individual LAN exposure with melatonin production and diurnal preference in day- and night-shift workers	75 night- and 42 day-shift workers, 22–64 years old, from 4 companies in Barcelona	Urine samples for all voids over 24-hr period for melatonin analysis. Diurnal preference assessed via Morningness–Eveningness Questionnaire. Light data loggers worn during waking hours	Light loggers worn at shoulder level but placed on a bedside table during sleeping, recorded levels every 12 or 15 min over 24-hr period	Night-shift workers experienced mean LE of 192 lux, day-shift workers mean LE of 57 lux, 22:00–07:00. Night-shift workers with daytime diurnal preference had 53.7% lower melatonin levels than those with evening preference. More evening shifts reduced suppression; with ≥ 9 night shifts, only 22.9% reduction

Note. 6-OHMS = 6-hydroxymelatonin sulfate (major urinary metabolite of melatonin); aMT6s = 6-sulfatoxymelatonin (indirect marker of melatonin production); cr = creatinine; LE = light exposure; *OR* = odds risk; TWA = time-weighted average.